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研究題目：Sugar Metabolism of *Scardovia wiggsiae*, a Novel Caries-Associated Bacterium

Scardovia wiggsiae has been detected from caries in children and adolescents and has been suggested to be a caries-associated microorganism. To investigate the cariogenic potential of *S. wiggsiae*, we examined carbohydrate metabolism and acid productivity, the fluoride sensitivity of carbohydrate metabolism and the mechanism by which fluoride inhibits carbohydrate metabolism, and the acid sensitivity of carbohydrate metabolism in this bacterium. *S. wiggsiae* metabolized glucose and reduced the environmental pH to 3.5（Figure 1）. It mainly produced acetic acid from glucose, together with small amounts of lactic and formic acid（Figure 2）. The 50% inhibitory concentration of fluoride for acid production was 8.0 mM at pH 7.0 and 1.5 mM at pH 5.5, which were much higher than those of representative caries-associated bacteria, such as *Streptococcus mutans*（Figure 2）. Metabolomic profiles showed the accumulation of 3-phosphoglycerate and a marked reduction in the pyruvate concentration in the presence of fluoride, suggesting that fluoride inhibits the latter half of glycolysis, including enolase activity（Figure 4）. Enolase activity was inhibited by fluoride in *S. wiggsiae*, but it was more fluoride-tolerant than the enolase activity of *S. mutans*. Unlike in *S. mutans*, lactic acid did not inhibit acid production by *S. wiggsiae* at acidic pH（Figure 3）. These results indicate that *S. wiggsiae* exhibits high acid production and tolerance to fluoride and lactic acid. *S. wiggsiae* possesses a unique metabolic pathway, the F6PPK shunt, which might allow it to avoid the lactate-formate pathway, including fluoride-sensitive enolase activity, and enable metabolic flow to the fluoride-tolerant acetate pathway. The fluoride tolerance of *S. wiggsiae's* enolase activity also increases the fluoride tolerance of its carbohydrate metabolism. The lactic acid tolerance of *S. wiggsiae's* acid production might result in *S. wiggsiae* having high acidogenic and aciduric potential and make it ecologically competitive in acidic environments, such as caries lesions, where lactic acid predominates.

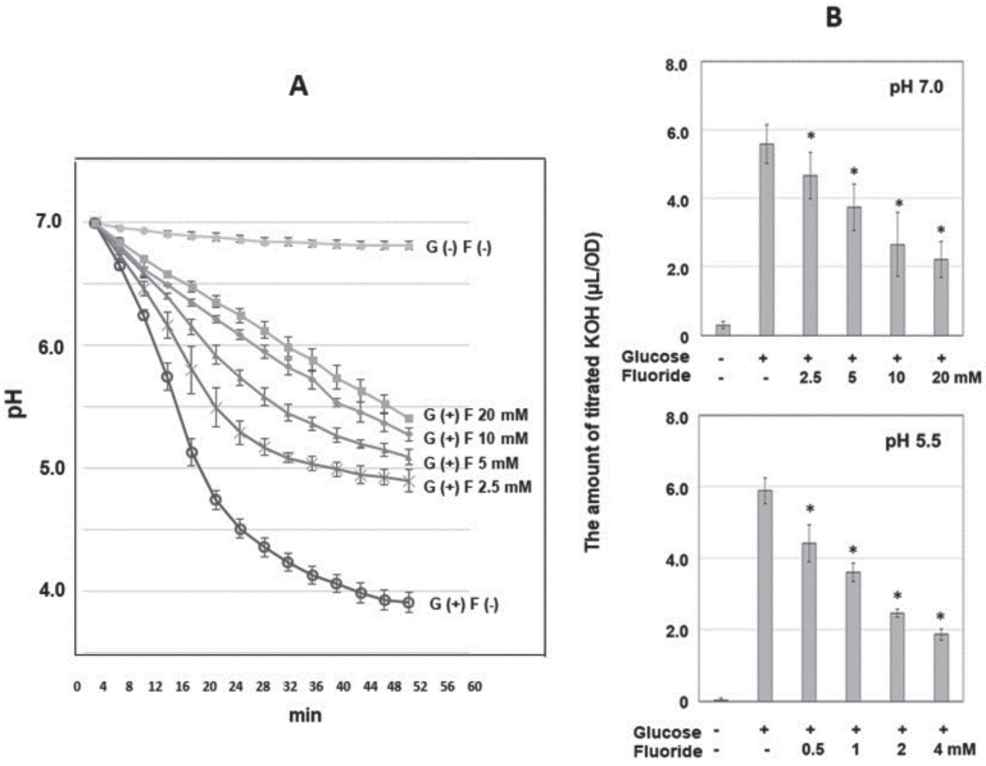
A
B
pH
7.0
6.0
5.0
4.0
G (-) F (-)
G (+) F 20 mM
G (+) F 10 mM
G (+) F 5 mM
G (+) F 2.5 mM
G (+) F (-)
0 4 8 12 16 20 24 28 32 36 40 44 48 52 56 60
min
The amount of titrated KOH (μL/OD)
pH 7.0
Glucose - + + + + +
Fluoride - - 2.5 5 10 20 mM
pH 5.5
Glucose - + + + + +
Fluoride - - 0.5 1 2 4 mM

Fig. 1

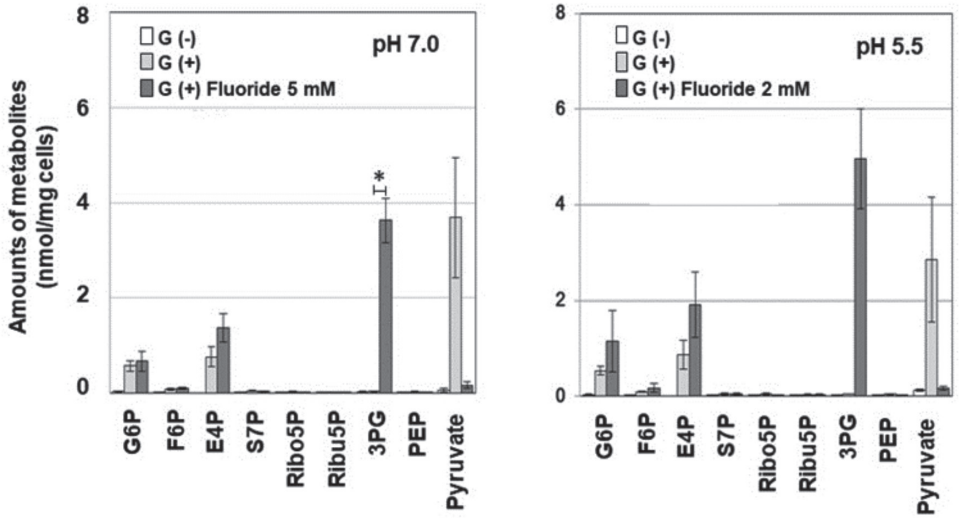
Amounts of metabolites (nmol/mg cells)
G (-)
G (+)
G (+) Fluoride 5 mM
pH 7.0
G (-)
G (+)
G (+) Fluoride 2 mM
pH 5.5
G6P
F6P
E4P
S7P
Ribo5P
Ribu5P
3PG
PEP
Pyruvate

Fig. 2

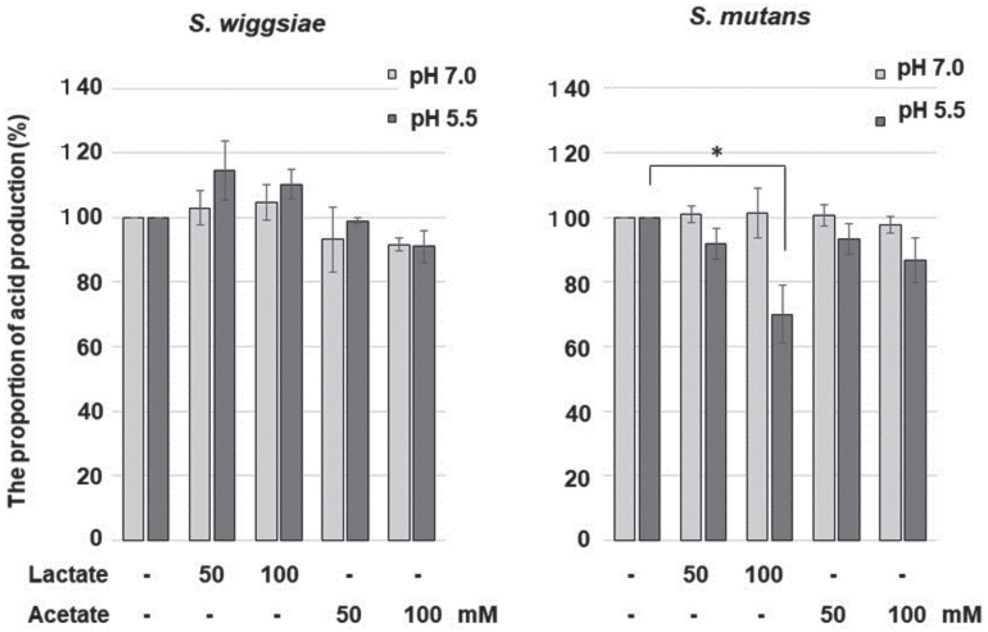
S. wiggsiae
S. mutans
pH 7.0
pH 5.5
The proportion of acid production (%)
140
120
100
80
60
40
20
0
*
Lactate - 50 100 - -
Acetate - - - 50 100 mM
- 50 100 - -
- - - 50 100 mM

Fig. 3

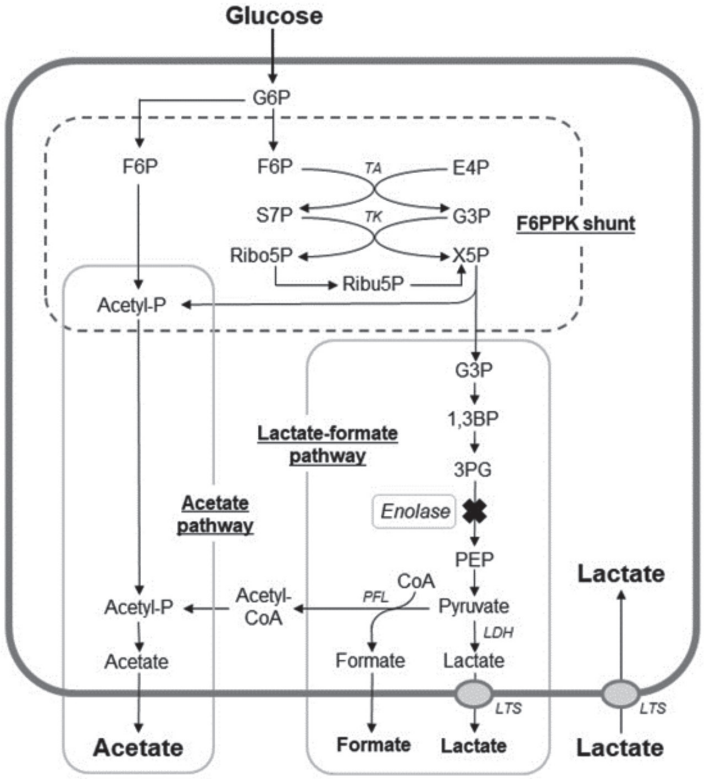
Glucose
G6P
F6P
F6P
TA
E4P
S7P
TK
G3P
F6PPK shunt
Ribo5P
X5P
Ribu5P
Acetyl-P
G3P
1,3BP
Lactate-formate pathway
3PG
Acetate pathway
Enolase
PEP
Lactate
CoA
Acetyl-P
Acetyl-CoA
PFL
Pyruvate
LDH
Acetate
Formate
Lactate
LTS
LTS
Acetate
Formate
Lactate
Lactate

Fig. 4

成果発表：（予定を含めて口頭発表、学術雑誌など）

- M. Kameda, Y. Abiko, J. Washio, Anne C.R. Tanner, Christine A. Kressirer, I. Mizoguchi, N. Takahashi: Sugar Metabolism of *Scardovia wiggsiae*, a Novel Caries-Associated Bacterium. *Front Microbiol.*（11: 479, 2020）
- Cariogenic potential of a novel caries-associated bacterium *Scardovia wiggsiae*, based on its unique carbohydrate metabolism・第16回インターフェイスサマーセミナー2021（2021年9月28日）
- Unique acid production from sugars and fluoride resistance of a novel caries-associated bacterium *Scardovia wiggsiae*・FJMU-HKU-TU International Symposium on Oral Health Sciences 2021（2021年11月18日）
- A novel ECC-related bacterium, *Scardovia wiggsiae*, has a unique carbohydrate metabolism with fluoride resistance・International Symposium for Interface Oral Health Science 2022（2022年1月15-16日）